June 10, 1955

Dear Dr. Demerec:

Thank you for sending the tabulations on your 4-point linkage test on tryD-10 cys B-12 x— try A8 me A18.

We were most interested to go over it— Dr, Morse and I particularly in some detail. After laboriously testing all the sequencies "geometrically" I worked out a "matrix" test in which this has been done once, and one can quickly analyze further batches of data. I enclose an explanation with some illustrations of its use; I am not sure how intelligible this will be, but once it is set up it saves a tremendous amount of time and mistakes.

The 3-point data you sent me went in fairly obvious fashion: I can easily understand the premises of your argument. The 4-point test unfortunately shows some discrepancies in regard to meth. In the En(cys,meth) for example, you show:

cys 362 cys-meth 365 cys-anth 1453 orig. cys-meth-(anth) 1453.

There seems to be a discrepancy as to whether there are 2 cys⁻meth⁻ or not.

Similarly, in the En(cys,meth,anth), there is cys 395 cys meth 397 but cys-anth 1635 cys-meth-anth 1635.

Was there a simple typographical error? These confused instances are the only suggestion of M⁻ types, which may throw some doubt on the linkage here, but to illustrate the use of the matrix method, I assumed the validity of cys⁻meth⁻ as a rare class.

In any event, largely because of the epistatis of tryD⁻ over tryA8, not all the sequences are excluded, and further experiments would be needed. Do my deductions correspond to your own.

My only general comment is that the analysis gives relatively little room to check internal consistency. I should think it would be extremely important to concentrate, for example, on a valid 4-point series, and to test this in all possible ways, not only by reciprocal transductions, but also by using different combinations of the markers as can be obtained from the transductions themselves. Otherwise, one can conclude that if the linear sequence model is correct, and there are no complications, then only one sequence will fit, but there will have been too little assurance that the sequence is in fact linear and unique.

Have you paid any attention to quantitative mapping? The data from a single transduction seem reasonably consistent, but I have not tried to handle the figures except as many/few, especially as I thought there was some question about part of the data. If you will reassure me about these, or want to discuss any other, I will be delighted to work on same.

Yours sincerely,

Joshua Lederberg

6/8: 1947
crossover notation 1/82